Sodium (23Na) and UTE MRI for Detection of Nerve Cell Injuries in Concussed Patients: Preliminary Study

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INTRODUCTION

A mild traumatic brain injury (mTBI) disrupts integrity of neurons and allows ionic flux across cell membrane, including efflux of potassium (K^+) and influx of calcium (Ca^{2+}) and sodium (Na^+). It may also result in stretching and tearing of nerve fibers (axons), causing delayed cell death[1]. These primary cellular-level injuries have not been directly targeted even by advanced MRI techniques such as DTI, SWI, fMRI or MRS[2], due to lack of proper investigative methodology. Measurement of these primary injuries will not only provide better understanding of subsequent (secondary) neuronal damages but also facilitate advance of clinical diagnosis, prognosis and management of mTBI or concussion. Here we proposed a new approach to detection of these primary cellular-level injuries using two recently-developed MRI techniques: (1) the intracellular sodium (^{23}Na) MRI for detecting acute disruption of nerve cell membrane and monitoring recovery or death of injured cells, and (2) the high-resolution (HR) ultrashort echo time (UTE) proton (^{1}H) MRI for detecting axonal tears due to stretching. Both techniques are noninvasive, three-dimensional (3D) and thus capable of detecting neuronal injuries anywhere in the brain, making each an ideal tool given the diffuse nature of mTBI/concussion. Very preliminary results are here presented from our study of two adolescent males with sports-related mTBI to demonstrate the feasibility of our idea.

METHODS AND EXPERIMENTS

Methods A single-quantum (SQ) sodium image at an ultrashort echo time (TE=0.5ms) is used to quantify total (or tissue) sodium concentration (TSC). A second SQ image at a short echo time (TE=5ms) is subtracted in magnitude from the first SQ image to produce a sodium image related to the short component of transverse (T2) relaxation. The short-T2 sodium image is used to quantify bound (or intracellular) sodium concentration (BSC) (more precisely, volume-fraction-weighted BSC or vBSC), under an assumption that bound sodium mainly locates in intracellular space in the brain. A HR-UTE proton image is used to highlight hard tissue against soft tissue or fluid in the brain to make stretching tears more visible. ***Experiments*** Two adolescent male patients, both age 16 with remote history of mTBI, diagnosed with sports-related mTBI (144 days and 17 days post-injury, respectively) were studied on a clinical 3T MRI scanner (Magnetom Trio Tim, Siemens Medical Solutions, Erlangen, Germany) with Tim head coil for proton imaging and a dual-tuned (^{1}H-^{23}Na) volume head coil (Advanced Imaging Research, Cleveland, OH, USA) for sodium imaging, under an approved IRB protocol. Sodium imaging used the TPI sequence[3] with FOV=220mm, matrix size=64, isotropic voxel size=3.44 mm, hard RF pulse=0.8ms, flip angle=80°, TR=100ms, TE1/TE2=0.5/5ms, p=0.4, TPI readout=36.32ms, total TPI projections=1596, averages=4, and TA=10.9×2 min. HR-UTE imaging used the AWSOS sequence[4] with TE/TR/θ =0.6/60ms/18º, 40 slices at 3mm thickness, FOV=220mm, matrix size=1024, resolution=0.22mm, spirals=256, spiral readout Ts=11.28ms, and TA=10.24min. As reference, a standard clinical protocol for mTBI was also implemented, including FLAIR, SWI, ADC, SPACE, and MPRAGE. ***Sodium quantification*** An integrated two-point linear calibration (CSF TSC=145mM, noise-only region TSC=0mM) was used for the quantifications of TSC and vBSC.

RESULTS AND DISCUSSION

Figure 1 shows an old lesion in the deep left frontal lobe with significantly lowered TSC (63.7±2.3 vs. 78.7±5.8 mM, p<0.001) and vBSC (36.6±4.7 vs. 42.9 ± 6.4 mM, p<0.001), suggesting tissue scarring. The region looks normal on standard proton images such as T1w-MPRAGE, FLAIR, SPACE and ADC where only evidence of an old bleed were visible on SWI. Figure 2 illustrates a long, thin stretching tear deep in the brain (17 days post injury). This suggests that stretching tears occurred in the brain and HR-UTE imaging was able to show them. These results collectively demonstrated that it is possible to detect primary cellular-level injuries in mTBI/concussed patients. However, so far we do not know whether these primary injures are common in concussed patients and how they relate to clinical symptoms. Our next step will be to study more patients and follow-up these primary cellular-level injuries to see how they are related to brain functioning and clinical symptoms.

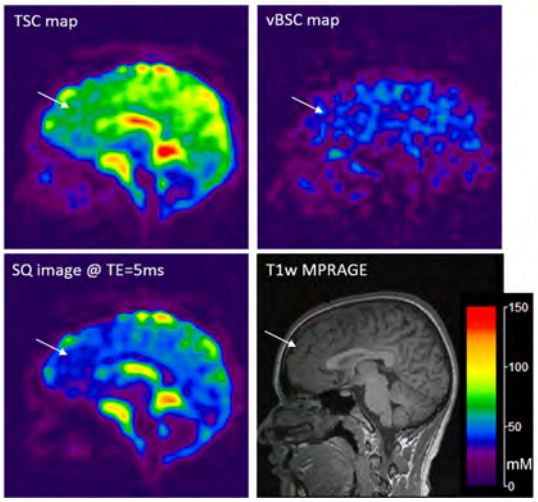

Fig.1. Sodium & proton images of a concussion patient, showing tissue scarring in deep frontal lobe with lower than normal values on both TSC and vBSC maps.

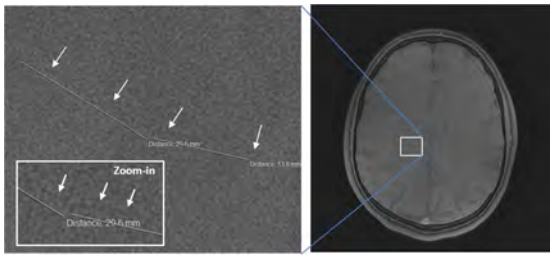

Fig. 2. HR-UTE image (res=0.22mm & TE=0.6ms) of a concussion patient at full (right) and zoomed-in (left) views, showing a fresh stretching tear of >34.4 mm long and 0.22-0.44 mm wide in the deep white matter region in the right side of the brain. (Zoom-in 3x for better view)

REFERENCES [1] Anderson T, et al. Pract Neurol 2006; 6:342-357. [2] Tate DF, et al. Brain Imaging Behav 2012; 6:103-107. [3] Boada FE, at al. MRM 1997; 37:706-715. [4] Qian Y, et al. MRM 2008; 60:135-145.